N-(4-{[2-(benzhydrylmethylamino)ethyl]methylamino}butyl)-3-(pyridin-3-yl)acrylamide.

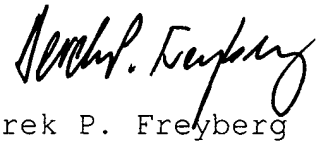
REMARKS

The Amendment

Entry of this amendment is respectfully requested. No new matter is added by the amendments, because the amended and new claims find support in the application as filed. In particular, the amendments to Claims 32, 33, and 41 correct typographic errors in those claims as filed, with the corrections evident from the application as filed, and the new composition Claims 45-49 correspond to method Claims 34-37 and 39, respectively, in compound scope.

Claims 32-49 are in this application, Claims 32, 33, and 41 having been amended, and Claims 45-49 having been added by this amendment. Entry of the amendment and allowance of the claims are requested.

Respectfully submitted,



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Attorney for Applicants
Reg. No. 29,250

Heller Ehrman White & McAuliffe LLP
275 Middlefield Road
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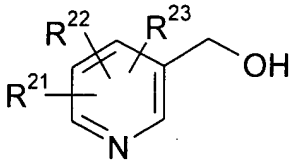
(650) 324-7014
November 16, 2001

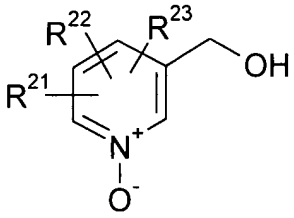
Amended claims showing amendments
(additions in bold, deletions in bold brackets)

32. (Amended) A method for preventing, reducing, or eliminating side effects or neutralizing the **[**effect**]** **side effects** of a cancerostatic or immunosuppressive agent administered prophylactically or therapeutically to a patient, comprising administering to the patient a compound having vitamin PP activity or a prodrug thereof.

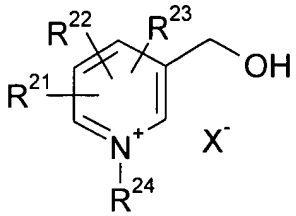
33. (Amended) The method of claim 32 where the compound having vitamin PP activity or a prodrug thereof is selected from the group consisting of compounds of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va, and Vb:



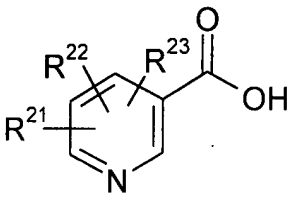
(II)



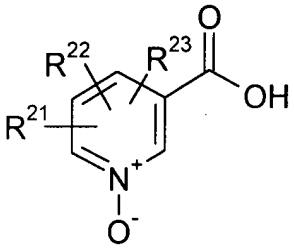
(IIa)



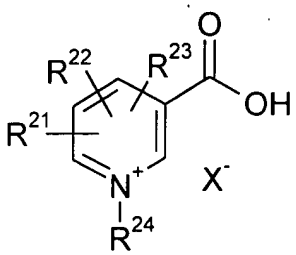
(IIb)



(III)



(IIIa)



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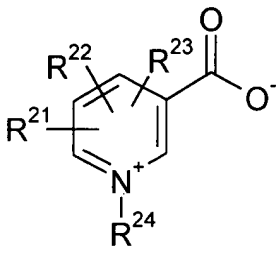
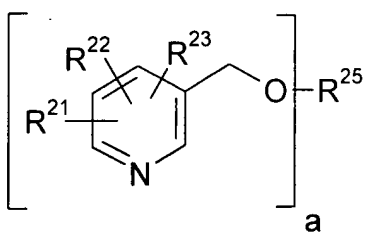
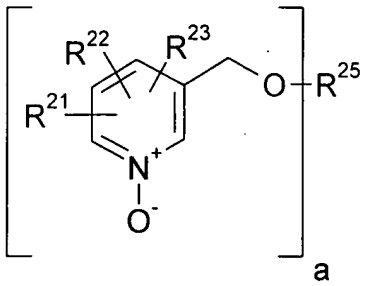


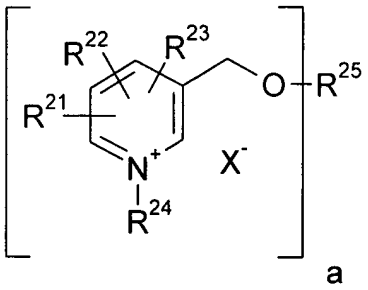
([IIIb] IIIc)



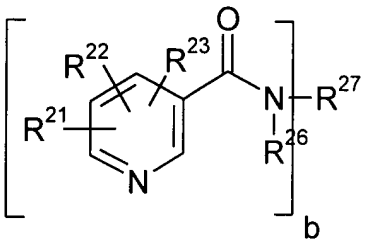
(IV)



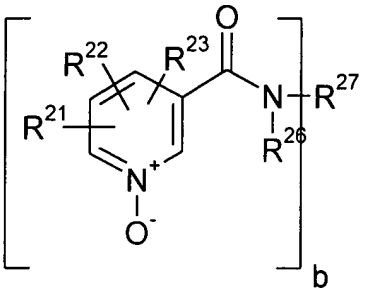
(IVa)



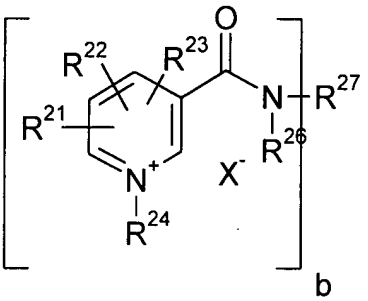
(IVb)



(V)



(Va)



(Vb)

where:

a is an integer of 1 through 6;

b is an integer of 1 through 2;

X^- is selected from the group consisting of fluoride, chloride, bromide, iodide, hydrogensulfate, mesylate, trifluoromethanesulfonate, tosylate, tetrafluoroborate, dihydrogenphosphate, and acetate;

R^{21} is selected from the group consisting of hydrogen, halogen, cyano, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, alkylthio, aminoalkyl, amino, alkylamino, dialkylamino, formyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, and carboxy;

R^{22} is selected from the group consisting of hydrogen, halogen, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, aminoalkyl, amino, alkoxycarbonyl, aminocarbonyl, and carboxy;

R^{23} is selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl;

R^{24} is selected from the group consisting of alkyl, alkenyl, hydroxyalkyl, alkoxyalkyl, and aralkyl;

R^{25} is such that the alcohol $R^{25}(OH)_a$ is selected from monovalent linear and branched C_{1-10} alkanols and ω-dialkylaminoalkanols, benzyl alcohol, divalent linear and branched C_{2-10} diols, mono- or divalent C_{5-7} cycloalkanols, C_{5-7} cycloalkanediols, C_{5-7} cycloalkanemethanols, saturated C_{5-7} heterocyclomethanols, tri-, tetra-, penta-, and hexavalent linear, branched, and cyclic alcohols with 3 to 10 carbon atoms, glycerin, 2,2-bis(hydroxymethyl)-1-octanol, erythritol, pentaerythritol, arabitol, xylitol, sorbitol, mannitol, isosorbitol, tetra(hydroxymethyl)cyclohexanol, and inositol;

R^{26} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 1, R^{27} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

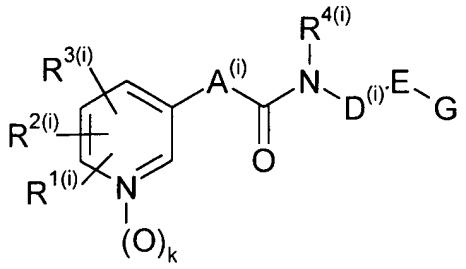
when b is 2, R^{27} is alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl;

and their thioxo analogs,

and the acid addition salts or anionic salts thereof.

41. (Amended) A pharmaceutical composition comprising:

(a) at least one compound selected from the group consisting of compounds of formula I:



(I)

where:

each of $R^{1(i)}$, $R^{2(i)}$, $R^{3(i)}$, and $R^{4(i)}$ are independently selected from the group consisting of halogen, hydroxy, trifluoromethyl, cyano, aliphatic hydrocarbyl residue optionally substituted with one or more functional groups and optionally interrupted by one or more heteroatoms, and aromatic hydrocarbyl residue; or $R^{1(i)}$ and $R^{2(i)}$ together form a bridge;

k is 0 or 1;

$A^{(i)}$ and $D^{(i)}$ are independently a saturated or unsaturated optionally substituted aliphatic hydrocarbyl residue, optionally interrupted by a heteroatom or a functional group;

E is a bond or is a heterocyclic residue having one or two ring nitrogen atoms or one ring nitrogen atom and one ring oxygen atom, linked to $D^{(i)}$ and G through a ring nitrogen atom and a ring carbon atom or through two ring nitrogen atoms; and

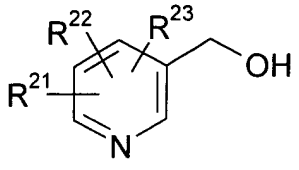
G is selected from the group consisting of hydrogen, an aliphatic or araliphatic residue, an unsaturated or aromatic monocyclic or polycyclic carbocyclic residue, a saturated, unsaturated, or aromatic monocyclic or polycyclic heterocyclic residue, bonded directly or through a functional group derived from a carbon, nitrogen, oxygen, sulfur, or phosphorus atom,

and the stereoisomers or racemic or non-racemic mixtures of stereoisomers thereof,

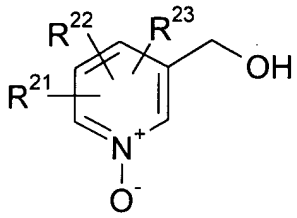
and the tautomers thereof when G is a heterocyclic aromatic ring or an aromatic ring substituted by a hydroxy, mercapto, or amino group,

and the pharmacologically acceptable acid addition salts thereof;

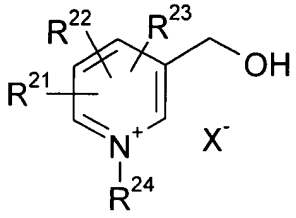
(b) at least one compound selected from the group consisting of compounds of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va, and Vb:



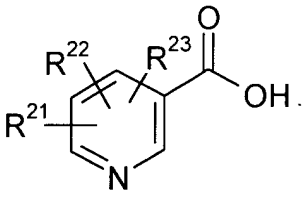
(II)



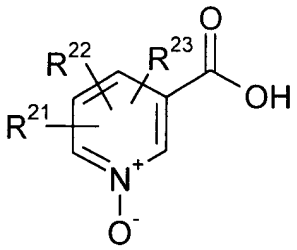
(IIa)



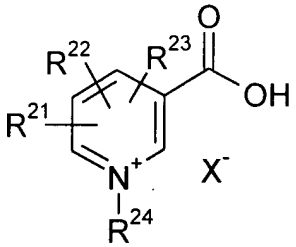
(IIb)



(III)



(IIIa)



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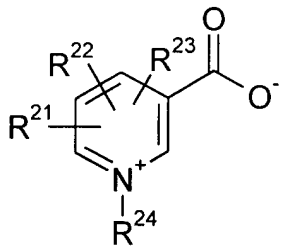
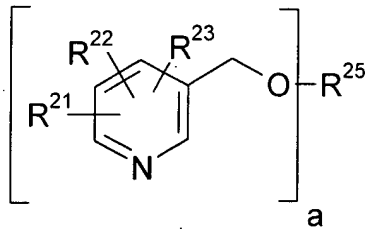


([IIIb] **IIIc**)



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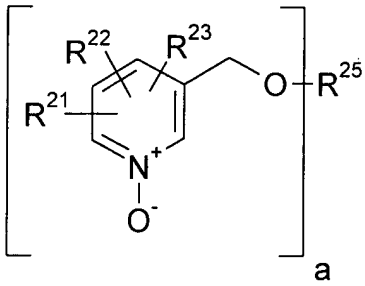
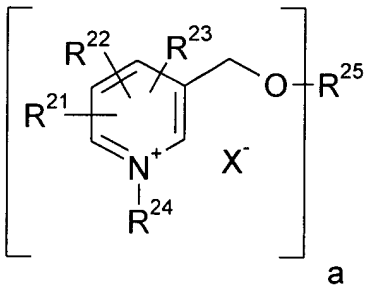


(IVa)



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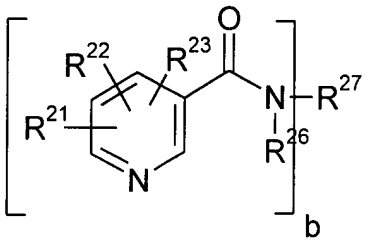
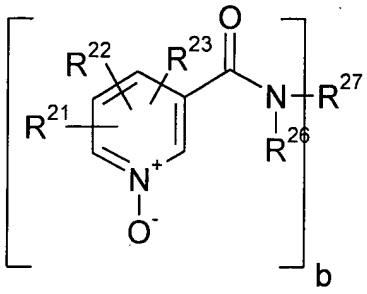
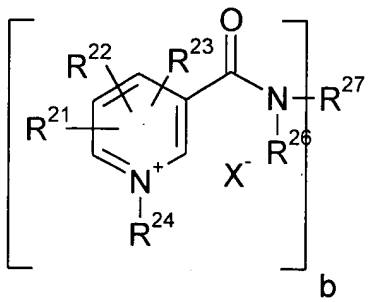


(V)



(Va)



(Vb)

where:

a is an integer of 1 through 6;

b is an integer of 1 through 2;

X^- is selected from the group consisting of fluoride, chloride, bromide, iodide, hydrogensulfate, mesylate, trifluoromethanesulfonate, tosylate, tetrafluoroborate, dihydrogenphosphate, and acetate;

R^{21} is selected from the group consisting of hydrogen, halogen, cyano, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, alkylthio, aminoalkyl, amino, alkylamino, dialkylamino, formyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, and carboxy;

R^{22} is selected from the group consisting of hydrogen, halogen, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, aminoalkyl, amino, alkoxycarbonyl, aminocarbonyl, and carboxy;

R^{23} is selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl;

R^{24} is selected from the group consisting of alkyl, alkenyl, hydroxyalkyl, alkoxyalkyl, and aralkyl;

R^{25} is such that the alcohol $R^{25}(OH)_a$ is selected from **monovalent linear and branched C_{1-10} alkanols and ω-dialkylaminoalkanols, benzyl alcohol, divalent linear and branched C_{2-10} diols, mono- or divalent C_{5-7} cycloalkanols, C_{5-7} cycloalkanediols, C_{5-7} cycloalkanemethanols, saturated C_{5-7} heterocyclomethanols, tri-, tetra-, penta-, and hexavalent linear, branched, and cyclic alcohols with 3 to 10 carbon atoms, glycerin, 2,2-bis(hydroxymethyl)-1-octanol, erythritol, pentaerythritol, arabitol, xylitol, sorbitol, mannitol, isosorbitol, tetra(hydroxymethyl)cyclohexanol, and inositol;**

R^{26} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 1, R^{27} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 2, R^{27} is alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl;

and their thioxo analogs,

and the acid addition salts or anionic salts thereof; and

(c) at least one physiologically acceptable carrier.